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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,371	04/08/2002	Gregor Cevc	2200437.120US1/VOS-020	1865

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WILMERHALE/BOSTON
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EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
04/03/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/890,371	CEVC ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-63 and 65-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-63 and 65-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicants' response to the office action mailed on 10/10/2007 was received on 1/8/2008 and has been entered into the record.

2. Claims 54-63 and 65-103 are pending and are the subject of this office action.

Specification

The specification remains objected to for having sections of text which are not readable. In the response received on 1/8/2008, the Applicants requested clarification regarding this objection. The Examiner's copy of the specification contains a region of text which is blank or otherwise obscured. Specifically, on page 27, in the paragraph spanning pages 26-27 (and starting on the 7th line from the top of the page), it appears that the page was obscured in some way during copying or scanning, rendering sections of text on the right side of the page unreadable. Because this paragraph discusses the preferred lipids of the invention, and the outstanding rejection under 35 USC 112, first paragraph is in regards to which lipids are suitable for use in the claimed composition, the Examiner requests a replacement page.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54-63 and 65-103 *remain rejected* under 35 USC § 112, first paragraph, regarding lack of enablement for a method of transnasally administering a composition comprising a penetrant comprised of any two substances other than a surfactant and a lipid, as set forth on pages 3-4 of the prior office action mailed on 10/10/2007.

The claims are drawn to a method for administering a pharmaceutical composition to a patient in need thereof, wherein said composition comprises an active ingredient and a carrier comprising a

penetrant suspended or dispersed in a solvent, wherein said penetrant is surrounded by a coating of at least one layer of two substances differing by at least a factor of 10 in solubility in a liquid medium, and wherein the less soluble substance is a lipid and the more soluble substance is a surfactant or a more soluble form of the lipid. In the office action mailed on 10/10/2007, the claims were found to not be enabled because the Applicants had previously asserted that compositions comprising didecanoyl-L-alpha-phosphatidylcholine would not be expected "to form a carrier with a penetrant including layers and aggregates with a diameter as claimed (and is expected to instead self-assemble into small aggregates in micellar form)". Because the specification did not teach what would differentiate a lipid which suitable for use with the claimed penetrant from those that are not suitable, the claims were found to be non-enabled.

In the response received on 1/8/2008, the Applicants argue that the specification is enabling because it provides information on how to prepare suitable penetrant compositions with lipids and surfactants as claimed, and the claims explicitly define in functional terms the properties of a suitable penetrant. The Applicants also assert that the specification lists various lipids and surfactants that are suitable for use in the claimed penetrants, and because sufficient guidance is provided in the specification and within the claims themselves, one of ordinary skill in the art would not require undue experimentation to select suitable materials for the claimed penetrant.

These arguments have been fully considered and are not persuasive. In the response to the previous office action mailed of 1/29/2007, the Applicants asserted that compositions comprising didecanoyl-L-alpha-phosphatidylcholine would not be expected "to form a carrier with a penetrant including layers and aggregates with a diameter as claimed (and is expected to instead self-assemble into small aggregates in micellar form)". The specification, on pages 26-27, lists exemplary lipids which may be used in the claimed penetrant, including phospholipids with the chemical formula shown on p. 26, where R_1 and R_2 are aliphatic chains, and typically C_{10-20}-acyl, -alkyl, or partly unsaturated fatty acid residues. Specifically preferred phospholipids include phosphatidylcholines (p. 27, line 10). Because didecanoyl-L-alpha-phosphatidyl choline is a phospholipid comprising 2 C_{10} (didecanoyl) unsaturated fatty acid residues, and has the same basic structure as that listed on p. 26, one of ordinary skill in the art would reasonably expect that didecanoyl-L-alpha-phosphatidyl choline would be an acceptable component of the claimed composition. However, although the instant specification provides guidance that would lead a skilled artisan to use phosphatidylcholines in the claimed penetrant, there is no guidance which would allow one of skill in the art to discriminate between phosphatidylcholines which would produce the claimed functional characteristics, and those which would not. Therefore, the mere listing of

various phospholipids in the specification does not provide the necessary guidance to one of ordinary skill in the art.

Therefore, because the claims read broadly on a penetrant comprising any lipid and surfactant composition comprising any lipid and surfactant that differ by a factor of 10 in solubility, and the lack of guidance in the specification which would allow one of ordinary skill in the art to determine which phospholipids, and phosphatidycholines in particular, which would be effective in the claimed composition, a person of ordinary skill in the art would require further, undue experimentation in order to make and use the claimed penetrant.

Claim Rejections - 35 USC § 112, first paragraph – written description

Claims 54-63 and 65-103 *remain rejected* under 35 USC § 112, first paragraph, regarding lack of written description for a method of transnasally administering a composition comprising a penetrant comprised of any two substances other than a surfactant and a lipid, as set forth on pages 4-5 of the prior office action mailed on 10/10/2007.

In the response received on 1/8/2008, the Applicants argue that the specification satisfies the written description requirement for the claimed genus of lipids and surfactants by an extensive listing of representative lipids and surfactants with common structural elements, and physical and chemical properties that are well-understood by those of skill in the art. Furthermore, the Applicants state that the claims recite specific functional characteristics required of any lipid or surfactant on the instant invention, including a recitation of a minute fluid droplet with a coating of at least two substances that differ by at least a factor of 10 in solubility, the substances forming aggregates with specified diameter limitations, the more soluble substance solubilizing the droplet, and/or the coated droplet having a particular elastic deformation energy. The Applicants also assert that the specification provides description of various penetrant compositions, including those comprising various phospholipids and surfactants. Therefore, due the disclosure of many types of useful materials, description of the composition of various penetrants, and the functional limitations of the claims, the claimed genus of penetrants has been adequately described by the specification.

These arguments have been fully considered and are not persuasive. As discussed *supra*, the Applicants have listed numerous phospholipids which are described as being useful in the claimed penetrant composition, including phospholipids having up to two aliphatic C_{10-20} unsaturated fatty acid side chains. The Applicants assert that didecanoyl-L-alpha phosphatidylcholine would not be an

acceptable lipid in the claimed composition. However, this phosphatidylcholine would seemingly be encompassed by the lipids listed on pages 26-27 by virtue of being a phospholipid having 2 R groups comprised of 10 carbon aliphatic fatty acids. Because one of ordinary skill in the art, based on the listings of pages 26-27 of the specification would conclude that didecanolyl-L-alpha phosphatidylcholine could be used in the claimed penetrant, but Applicants assert that this particular phosphatidylcholine could in fact not be used, the specification does not adequately describe in structural or chemical terms what attributes are required of phospholipids of the instant invention. In other words, there is no description in the specification of chemical or structural requirements of lipids that would (a) produce the claimed functional characteristics recited in claims 54 and 103, and (b) differentiate functional lipids from those that would not be functional in the claimed penetrant composition.

Conclusion

No claim is allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571)272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce D. Hissong
Art Unit 1646

/Robert Landsman/
Primary Examiner, Art Unit 1647